Please amend the claims as follows:

45. (amended) A method of inhibiting tumor cell invasion, reducing the viability of melanoma cells and inhibiting melanoma cell growth in an animal comprising administering to an animal a therapeutically or prophylactically effective amount of an antisense compound 8 to 30 nucleobases in length targeted to a coding region or a 5'-untranslated region, a start codon region, a coding region, a stop codon region or a 3'-untranslated region of a nucleic acid molecule encoding focal adhesion kinase of SEQ ID NO: 1.

55. (amended) The method of claim 45 wherein said antisense compound is administered in combination with a therapeutically or prophylactically effective amount of 5-fluorouracil.

REMARKS

Claims 45-58 are pending in the instant application. Claims 45-58 have been rejected. Claims 56-58 have been canceled. Claims 45 and 55 have been amended. No new matter has been added by these amendments. Reconsideration is respectfully requested in light of these amendments and the following remarks.

I. Double Patenting

Claims 45-54 have been rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 27 and 28 of U.S. Patent 6,133,031. The Examiner suggests that although the conflicting claims are not identical they are not patentably distinct because they overlap in scope. Specifically, the Examiner suggests that instant claims 45-54 would encompass the narrower methods of treating neovascularization in patented claim 28 and would encompass methods of inhibiting expression of focal adhesion kinase of patented claim 27. Applicants have amended the claims as discussed below to specify that the method of the instant invention is for inhibiting tumor cell invasion, reducing the viability of melanoma cells or inhibiting melanoma cell growth. Neither claims 27 nor 28 of U.S. Patent 6,133,031 specify these particular uses or include these particular uses. Accordingly, withdrawal of this rejection is respectfully requested.

Claims 45, 46 and 48-54 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 6 and 16 of copending Application No. 09/615,352. Although the conflicting claims are not identical, the Examiner suggests that they are not patentably

distinct. Applicants respectfully request that this rejection be held in abeyance until one of the applications has been allowed as the scope of the claims may change during prosecution.

II. Rejection of Claims Under 35 U.S.C. 112, First Paragraph

Claims 45-58 have been rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims. The Examiner suggests that the specification while being enabling for a method of inhibiting neovascularization in the eye using an antisense molecule targeted to human focal adhesion kinase and inhibiting growth of melanoma tumors using antisense targeted to human focal adhesion kinase of SEQ ID NO: 18, does not reasonably provide enablement for generally treating any disease or condition associated with focal adhesion kinase, or any cancer using antisense targeted to human focal adhesion kinase. Further, the Examiner suggests that the specification fails to enable use of any chemotherapeutic compound in conjunction with SEQ ID NO: 18, other than 5-fluorouracil. The Examiner cites several articles to

support the position. Applicants respectfully traverse this rejection of the claims.

At the outset, Applicants have amended claims 45 and 55, and their dependent claims, to recite that the invention is a method of inhibiting tumor cell invasion, reducing viability of melanoma cells or inhibiting melanoma cell growth and, that the chemotherapeutic used is 5-fluorouracil, and that the compounds are targeted to specific region of the human FAK of SEQ ID NO: 1, in an earnest effort to advance the prosecution and facilitate the allowance of this case. Claims 56-58 have been canceled. Support for these amendments to the claims can be found throughout the specification as filed but in particular at pages 51-56.

Applicants respectfully disagree with the Examiner's suggestion that cited references on antisense technology support the position that application of antisense *in vivo* is unpredictable.

The Examiner has pointed to three articles on the technology of antisense oligonucleotides to support the view that antisense technology is unpredictable. However, when one reads each of these papers as a whole, as required under MPEP 2141.02, these references actually teach the potential usefulness of this class of drugs in humans, and more importantly fail to provide any reasonable basis

to doubt the pharmacological activity observed in cells or *in vivo* in animals in the instant invention would also occur in cells or *in vivo* in animals and humans when antisense compounds targeted to FAK other than SEQ ID NO: 18 are employed.

The paper by Branch (1998) teaches the need to develop antisense molecules based on sound data and careful screening, such as presented in the instant specification. Nowhere does the paper state that extrapolation from *in vitro* data to *in vivo* effects is unpredictable. Nor does this paper state that data from *in vivo* studies on a particular compound are not predictive of pharmacological activity *in vivo* for related compounds.

The paper by Green et al. (2000) is another review of the science of antisense and even discusses some of the clinical trials that are ongoing with antisense compounds. Nowhere does the paper state that extrapolation from *in vitro* data to *in vivo* effects is unpredictable. Again, this paper fails to state that data from *in vivo* studies on a particular compound are not predictive of pharmacological activity *in vivo* for related compounds.

The paper by Jen and Gewirtz (2000) also discusses the science of antisense technology and the fact that antisense is one of the tools currently being used to suppress gene expression. Nowhere

does the paper state that extrapolation from *in vitro* data to *in vivo* effects is unpredictable. As with the other two papers cited, this paper also does not state or suggest that data from *in vivo* studies on a particular compound are not predictive of pharmacological activity *in vivo* for related compounds.

Development of antisense drug products is viewed by those of skill in the art as being the same as development of any other drug product in terms of applying the basic principles of pharmacology. The key is the careful design of the *in vitro* and *in vivo* studies to carefully evaluate dose-response relationships and antisense mechanism, similar to the type of studies presented in the instant specification. In the specification as filed, studies are presented where pharmacological activity of compounds related to SEQ ID NO: 18 also have activity that would allow them to inhibit tumor cell invasion, to reduce viability of melanoma cells and to inhibit melanoma cell growth. Therefore, when antisense oligonucleotides are developed using well designed studies that progress logically from activity in cells to activity in animals and humans, one of skill would expect that activity in cells would be predictive of activity *in vivo*, and further that activity *in vivo* with one compound of a class (SEQ ID NO: 18) would be

predictive of pharmacological activity of other compounds of that class, *i.e.*, FAK expression inhibitors.

Based on the amendments to the claims and these remarks, withdrawal of the rejection is respectfully requested.

III. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE**."

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claims 56-58 have been canceled.

Claims 45 and 55 have been amended as follows:

45. (amended) A method of ~~treating an animal having a disease or condition associated with focal adhesion kinase~~ inhibiting tumor cell invasion, reducing the viability of melanoma cells or inhibiting melanoma cell growth in an animal comprising administering to ~~said~~ an animal a therapeutically or prophylactically effective amount of an antisense compound 8 to 30 nucleobases in length targeted to a 5'-untranslated region, a start codon region, a coding region, a stop codon region, or a 3'-untranslated region of a nucleic acid molecule encoding focal adhesion kinase of SEQ ID NO: 1.

55. (amended) The method of claim 45 wherein said antisense compound is administered in combination with a therapeutically or prophylactically effective amount of ~~a chemotherapeutic agent~~ 5-fluorouracil.